

AMENDMENTS TO THE SPECIFICATION

Please delete the existing Sequence Listing and substitute therefore the accompanying Sequence Listing (pages 1-2).

At page 13 amend paragraph 0038 as follows:

[0038] Figure 7A: The nucleotide sequence (in a 5' to 3' orientation, SEQ ID NO:2 and its complement SEQ ID NO:3) (~~SEQ ID NO:2~~) of the HD-PNA is bordered on the amino terminus by a biotin (bio) residue and by tyrosine (Y) and lysine (K) residues at the carboxyl terminus. There are five linkers (designated O) flanking the nucleotide sequence. The complementary nucleotide sequence of the HD target mRNA (in a 5' to 3' orientation) is shown and the methionine initiation codon (ATG) is underlined. The HD exon 1 sequence is downstream of the T3 RNA polymerase promoter which allows for in vitro transcription of HD exon 1 mRNA. Figure 7B: Combined in vitro transcription/translation assays resulted in the formation of ³H-labeled exon 1 huntingtin protein that was precipitated by trichloroacetic acid (TCA). The translation of the HD exon 1 protein was inhibited in a dose response by either a PO-ODN (III) or by the PNA. (C) The RNase protection assay (RPA) demonstrates formation of an HD mRNA protected fragment following complete nuclease digestion, owing to hybridization of the biotinylated HD PNA to the huntingtin exon 1 mRNA (lane 2). The conjugation of the antisense PNA to the MAb-SA transport vector does not inhibit the hybridization of the PNA to the target mRNA, based on the formation of the RNase protected oligonucleotide shown in lane 4. Conversely, no protected fragment is observed following mixing of an anti-luciferase (Luc) PNA with the HD RNA, either in an unconjugated form (lane 3) or conjugated to the MAb-SA vector (lane 5). BPB = bromophenol blue.

At pages 31-32 amend paragraph 0112 as follows:

[0112] In another approach, the nucleic acid comprising the reagents of this invention can be substituted with a "knockout construct" capable of binding to and inserting itself in a target gene or gene promoter and thereby disrupting expression of that gene. Such disruption can be specifically directed to a target gene by homologous recombination where a "knockout construct" contains flanking sequences complementary to the domain to which the construct is targeted. Insertion of the

knockout construct. ~~into a~~ into the target gene or promoter results in disruption of expression of that gene.